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PROCESS TO REVISE GUIDELINES
The original guidelines were developed using a consensus process involving representatives from various disciplines and settings, including palliative care specialists and non-specialists with significant experience in palliative care.

The guidelines will be reviewed every three years by the Champlain Hospice Palliative Care Program (CHPCP) Clinical Advisory Committee. This process will include a review of international peer reviewed literature related to the topic as well as sample local, national and international guidelines. Any suggested revisions made by the Clinical Advisory Committee will be circulated broadly to representatives across the region from various disciplines and settings for input and review before being adopted.

EDITORIAL INDEPENDENCE:
• This guideline was developed without external funding
• The developers have declared an absence of conflict of interest
INTRODUCTION

Palliative Sedation Therapy (PST) is to be considered as a last resort option when all other treatments have failed. It should not be confused with sedation that results as an adverse side-effect from treatment of a symptom. PST begins when the intention or goal of treatment is to achieve sedation in a patient who is at the end of life and has a symptom(s) that cannot be controlled. This guideline supports the use of proportional sedation, and includes guidance on monitoring as an appendix.

The inter-professional community of palliative care professionals in Ottawa and the Champlain Region recognizes the importance of palliative sedation therapy-related clinical guidelines in order to ensure that this therapy is applied and monitored appropriately. This is also supported by the literature. The primary goal of the guidelines, including the medication protocols, is to ensure effective, safe and appropriate use of palliative sedation therapy in the Champlain region. They also aim to enhance standardization of practice, as it relates to PST. It is recognized that there exists considerable literature on PST. The goal of these Champlain Guidelines is to provide the essential elements as identified through the consensus process and support daily clinical practice.

With the goal of symptom relief not death, and use of interventions proportional to symptom severity, it is emphasized PST is unrelated to the process of Medical Assistance in Dying (MAID) and the literature indicates that when used appropriately palliative sedation does not hasten death.

Consultation with a palliative care team is recommended prior to initiation of PST. This is particularly crucial if continuous deep sedation is anticipated.

DEFINITIONS

Palliative Sedation Therapy (PST)
Therapeutic (or palliative) sedation in the context of palliative medicine is the monitored use of medications intended to induce a state of decreased awareness or absent awareness (unconsciousness) in order to relieve the burden of otherwise intolerable suffering for terminally ill patients in a manner that is ethically acceptable to the patient, family and health-care providers.

Proportional Sedation
Although PST may be associated with a deep level of sedation, some patients may find relief of their intractable symptom(s) at a light or moderate level of sedation. Given the variations in the clinical presentation of the problem and the broad inter-individual variability in response to the medication(s) used in PST, doses of the medication(s) are usually titrated to achieve the required goal, namely comfort and alleviation of the refractory symptom(s). The aim is to use the lowest dose of medication that achieves this goal. In some patients, symptom(s) relief may be achieved at a light level of sedation with small doses of medication. In others, comfort can only be achieved at a deeper level of sedation with higher doses of medication. Titration of the dose to achieve the goal is therefore essential.
**Refractory/ intractable symptom(s)**

“The diagnostic criteria for the designation of a refractory symptom(s) include that the clinician must perceive that further invasive and non-invasive interventions are (i) incapable of providing adequate relief, or (ii) associated with excessive and intolerable acute or chronic morbidity or (iii) unlikely to provide relief within a tolerable time frame.” Interventions must also be acceptable to the patient (or substitute decision maker (SDM) if the patient is not mentally capable) and consistent with current goals of care.

**FORMAT**

The clinical practice guidelines are divided into two sections: General Guidelines and Medication Guidelines.

**General Guidelines for Palliative Sedation Therapy:** The general guidelines further define refractory symptoms and outline various types of sedation to clarify what palliative sedation therapy (PST) is. Common indications for PST and the criteria that need to be in place before PST is initiated in a particular patient are identified. The guidelines apply to a variety of settings of care, including in-patient medical and surgical units, in-patient palliative care units, hospices, patient homes and nursing homes.

**Medication Guidelines for Palliative Sedation Therapy:** This section of the Guidelines relates specifically to the medications used for achieving palliative sedation therapy. Though comparative studies of various medication protocols are not currently available the literature is used to guide recommendations.

**GENERAL GUIDELINES FOR PALLIATIVE SEDATION THERAPY**

Given the goal of symptom(s) control, these guidelines emphasize the importance of using proportional sedation, where the degree of sedation is titrated to achieve symptom(s) control. Thus PST does not necessarily imply deep sedation to unconsciousness. In some cases, light sedation may achieve adequate symptom(s) control while permitting ongoing oral intake and communication. Identifying the goals of the therapy and having tools in place to monitor its effect are critical.

**Indications for Palliative Sedation Therapy**

Most common indications: 3,13,21

- Intractable dyspnea
- Intractable delirium
- Intractable seizures
- Other Intractable physical symptoms: pain, nausea etc.

Less common indications: (these may require additional consideration):

- Intractable existential/spiritual suffering
- Intractable psychological suffering
Determining if a “Refractory Symptom” is Present
Prior to the introduction of PST it is essential to identify the symptom(s) and determine if the symptom(s) is refractory (see Figure 1). It is important that those assessing if a symptom is refractory have adequate knowledge of the patient and experience to make this determination.\textsuperscript{23} It can be particularly difficult to ascertain whether or not a psychological, spiritual, existential or social source of suffering is refractory.

Whenever possible, using an inter-professional team that includes physicians and nurses trained in palliative care, social work, spiritual care, and a psychologist and/or psychiatrist, is advised. This team would work with the patient to address their distress and help determine if this criterion is met. It is recognized that the assessment and management of these types of suffering take longer and are often more complex than that for physical symptoms. Use of light or intermittent sedation to address suffering may be considered.

While it may be determined that a symptom is refractory and that PST may be an option, it is important that the patient (or their Substitute Decision Maker if the patient is not mentally capable) give consent to the treatment and that PST is within current goals of care.
*In this context “unacceptable” and “reasonable” must consider the perspective of the patient, (or substitute decision maker when appropriate). If palliative sedation therapy is determined to be an option, appropriate consent must be obtained and documented before proceeding.
For the purposes of this set of guidelines, PST will be distinguished from other forms of sedation. (See Figure 2):

**Fig. 2 Types of medication-induced sedation**

*Temporary use of sedation where the underlying causes of the symptom(s) are reversible and attempts are being made to treat these causes is not considered PST as once it is felt that underlying causes have been reversed, sedation is withdrawn. **If the causes are not reversed and a decision is made to continue with sedation indefinitely, sedation then by definition becomes PST and should be documented as such.**

It is also important to recognize that increasing somnolence and loss of consciousness are also natural end-of-life phenomena. This natural dying process may be responsible for somnolence and reduced levels of consciousness even in the absence of medications such as opioids or neuroleptics. As per usual good medical practice, the risks and benefits of any treatment must be considered and regular assessment of their effects is critical.
CRITERIA AND PROCESS

Criteria
Each of the following criteria needs to be met prior to considering PST: 5,14,23, 25
1. A progressive, incurable illness is present with a limited life expectancy. In all but the most unusual cases for deep sedation, death must be imminent within days.
2. The presence of a refractory/intractable symptom(s) or symptom(s)
3. All reasonable attempts have been made to control symptom(s) using other interventions. The primary attending care team shall ensure that a palliative care inter-professional team (where available) and/or another physician is consulted to review the case where deep sedation is planned.
4. Informed consent of the patient or his/her surrogate decision maker must be obtained and documented.
5. Goals of care should be carefully reviewed. In most cases, A "Do not resuscitate" (DNR) order would be anticipated. i.e. the patient agrees that the team will allow a natural death to occur. Exceptions may apply if lighter levels of sedation are being used. This must be clearly documented.

Process
In addition to the above criteria, the most responsible provider should undertake the following process steps both before PST is initiated and once it is in place:
1. Ensure the above criteria are met and the rationale for considering and/or initiating PST is documented in the patient chart.
2. Document results of discussion about artificial nutrition and/or hydration and any associated plan (see below in “other considerations”)
3. Determine and document the target level of sedation
4. Ensure monitoring guidelines with appropriate documentation are in place.

OTHER CONSIDERATIONS

Medications
The medication regimen that was required to control symptoms prior to initiating PST should be continued. Oral medications should be changed to a non-oral route depending on the patient’s level of consciousness and ability to take and absorb oral medications. Other medications should be reviewed and possibly discontinued if not essential to the patient’s comfort.

Hydration and Nutrition
Gradual cessation of fluid and food intake is generally considered normal and expected when patients are approaching end-of-life. The majority of patients will have minimal to no oral intake by the time Palliative Sedation Therapy (PST) is considered. If the patient is still able to take fluids and/or food, the physician must discuss the consequences of initiating moderate to deep continuous sedation on the patient’s ability to continue taking fluids and/or food by mouth. If the patient and/or family express a desire to continue taking fluids and/or food by mouth, then light or intermittent sedation may be considered as an alternative to deep continuous sedation.
Artificial nutrition and hydration are often considered burdensome and to offer minimal benefits in patients who are actively dying. There is also risk of side effects. Therefore they should not be routinely offered to patients undergoing PST.

The physician must review the appropriateness, benefits and burden of continuing artificial hydration and nutrition while undergoing PST for patients who are currently receiving artificial hydration and/or nutrition.

**Bladder monitoring**
When initiating moderate to deep sedation, consider the placement of a urinary catheter. The catheter should be inserted once the patient is sedated, to avoid discomfort of placing the catheter. If the decision is made to not insert a urinary catheter, health care providers must regularly assess the patient for urinary retention.

**Bowel assessment**
Continue to monitor bowel function and consider intervention if appropriate based on assessment and goals of care.

**Positioning**
Regularly assess positioning and adjust as appropriate based on current nursing best practice.

**MEDICATION GUIDELINES FOR PALLIATIVE SEDATION THERAPY**

The literature does not provide evidence supporting a particular medication protocol for PST. Suggestions below are based on the information available in the literature and consensus opinion.

*Both literature and regional consensus confirm that opioids should not be used for PST.*

Midazolam (Versed™) as a continuous infusion is the method of choice for PST in most guidelines. This is likely due to its potency, short half-life and the ability to titrate the dose up or down fairly rapidly. It also has amnesic properties. The subcutaneous (subcut.) route is usually preferred, although intravenous use may be considered if a patient already has a central /PICC line. It is recognized that in some settings, access to a pump for continuous infusion is not readily available. In that case, midazolam may be administered intermittently on an hourly basis. Alternatively, the use of other agents such as phenobarbital, sedating neuroleptics such as methotrimeprazine or longer acting benzodiazepines such as lorazepam have been documented in the literature.

It is recognized that some of these drugs may be used in palliative care for indications other than PST. In the context of PST, the medications cited are used specifically with the intent of inducing sedation where the symptom(s) is deemed to be intractable and irreversible. It is also recognized that the realities of different settings (e.g. in-patient palliative care unit versus patient's home) influence the medication and protocol used.
Option 1: Midazolam by continuous infusion. (This is the preferred option)

- Determine target degree of sedation (see appendix A)
- If deep sedation is the goal, consider adding a loading dose of midazolam: 2.5-5mg subcutaneously (subcut.) or intravenous (IV).
- Continuous infusion of midazolam: Starting range 0.2-1mg/hour subcut or IV infusion via an infusion pump.25
  - Consider including an as needed dose to help achieve or maintain target sedation (can use the hourly rate every 30 minutes if needed)
- Titrate up (or down) every 30 minutes if needed until the goal is achieved.*
- The initial titration may need to be rapid until the patient is comfortable, using appropriate monitoring. The rapid onset of action (5-15 minutes) and peak within 60 minutes allows this. Mean duration of action is 2 hours, but can be longer (up to 6 hours) particularly with renal failure, congestive heart failure (CHF), cirrhosis, and in the elderly. Half-life varies from 1.8 to 6 hours (Lexi-comp). A plan for reassessment and titration will need to be determined considering the resources available.
- Once the goal is achieved, the dose is maintained. (The usual dose required to achieve PST is between 1 mg/hr. and 6mg/hr.)
- Monitoring continues on a regular basis to ensure that the target degree of sedation is maintained. Over time (usually many hours to days) the dose may need to be increased by titration (as above) to achieve an appropriate level of comfort as some patients may develop tolerance to the midazolam.

*If doses of greater than 10mg/hr. are required, consider adding another agent such as methotrimeprazine or phenobarbital. See doses below. ***A very small group of patients may experience a paradoxical reaction to midazolam (i.e. agitation)

Option 2: Methotrimeprazine (Nozinan™)

- Determine the desired degree of sedation (see Appendix A)
- Administer an initial dose of methotrimeprazine 5-25mg subcut (depending on degree of sedation desired and individual patient factors)
- Follow up with methotrimeprazine 5-25mg subcut q8hrs and q2 hours as needed. In most cases, the higher dose (25mg) is required if deep sedation is the intent.
- The dose may be increased to a maximum of 25mg subcut q6 hrs. to achieve the target level of sedation.
- If higher doses than this are required, consider switching to midazolam (option 1) if not already in place or adding phenobarbital (option 3)
Option 3: Phenobarbital

- Determine the desired degree of sedation (see Appendix A)
- If deep sedation is the goal consider adding a loading dose of phenobarbital 120 mg.
- Based on goals, administer phenobarbital 30mg, 60 mg, 90mg or 120 mg deep subcut. (use the higher dose in a situation of extreme suffering and/or where deep sedation is planned)
- Based on response and target sedation continue with regular dosing twice daily.
- Titrate the phenobarbital dose until goal reached. Maximum dose is 720 mg in 24 hours (240 mg subcut TID).

The half-life of phenobarbital is very long (53-118 hours). This means that several days need to pass (to achieve steady state) before the full impact of a specific dosing regimen can be adequately assessed. Use with caution if a lighter level of sedation is desired.

Option 4: Combination of medications

- When single medication approaches above have failed or are suboptimal, the medications may be combined.

Option 5: Propofol

- Propofol is a powerful anesthetic agent and for PST can only be used by those knowledgeable about its use in settings in which it is approved and where appropriate monitoring and support is available.

TITRATION AND MAINTENANCE OF SEDATION

Continue to monitor and adjust medications to achieve the desired goal. Use the lowest dose of medications and aim for the lightest level of sedation possible that achieves patient comfort. Over time, doses may need to be increased due to changes in the disease/its complications, or the development of tolerance to the sedative agent. Sometimes doses may need to be reduced when it is apparent that the level of sedation is excessive for the desired goal. Titration is also influenced by the availability of clinical staff. In an in-patient palliative care unit, midazolam infusions may be titrated every 30 minutes with the appropriate monitoring (see Patient Monitoring section). This may not be possible in a home setting if there is no experienced nurse or physician available.

It is understood that an acute crisis may arise in some conditions requiring very rapid titration (e.g. intractable delirium in which the patient may harm himself or others, or strider secondary to tracheal obstruction). In those situations, sedation may be initiated at a deeper level and later adjusted if the condition stabilizes.
PATIENT MONITORING

The frequency of patient monitoring and the parameters to be monitored is influenced by the setting, circumstances and the availability of clinical staff.

For most patients near end of life, formal assessment of PST and documentation using RASS-PALL will be in conjunction with regular monitoring, which is generally recommended to occur at least every hour near end of life. In home or other community settings, it is essential to ensure that adequate supports are available and that if family members are responsible for monitoring that they have adequate teaching and rapid access to health care professionals. Many family members and other team members experience significant distress when a loved one or patient is receiving PST. It is important to provide them with emotional support and address any concerns they may have.

Parameters for routine monitoring include:

1. The level of sedation:

   We recommend the use of the RASS-PAL (Richmond Agitation Sedation Scale, Palliative), **attached as Appendix A** to standardize the assessment method and provide physicians and nurses with a standardized method of communicating about PST, assessing the effectiveness of treatments, and setting treatment goals.

2. Ongoing symptom monitoring:

   Assess the degree to which the patient reports (if he/she is able to) symptoms are controlled. If able, the use of the ESAS (Edmonton symptom(s) assessment system) or other structured symptom(s) monitoring tool can be continued. If the patient is unable report symptoms, the clinician or nurse must assess what they perceive the patient's level of comfort or discomfort to be. If it appears that the patient is becoming more uncomfortable, reassess the patient for any causes for the discomfort that may have been missed or started since the last assessment (e.g. urinary retention).

Other parameters may be assessed on a case-by-case basis; this includes decisions about whether or not to monitor respiratory rate and oxygen saturations. It is important to note that changes in respiratory rates and patterns, as well as reductions in oxygen saturation also occur normally at end-of-life.

Any assessments should be documented in the patient chart.
## Frequency of PST monitoring (recommend using RASS-PALL)

<table>
<thead>
<tr>
<th></th>
<th>In-patient settings</th>
<th>Home, Residential or Long-Term Care Settings (family caregivers may require teaching)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initiating PST</strong></td>
<td>Monitor every 30 minutes until the goal of PST is achieved.</td>
<td>Initial titration will require nursing support*: Monitor every 30 minutes until the goal of PST is achieved.</td>
</tr>
<tr>
<td></td>
<td>Continue monitoring every 30 minutes until the target symptom is controlled without requiring additional PRN doses or dose titrations up or down for one hour. Then monitor q 4hrs.</td>
<td>Continue monitoring every 30 minutes until the target symptom remains controlled without requiring additional PRN doses or dose titrations up or down for one hour.</td>
</tr>
<tr>
<td><strong>Maintaining PST</strong></td>
<td>Monitor q 4hrs.</td>
<td>Monitor q 8hrs.</td>
</tr>
<tr>
<td>Any dose adjustments made or additional bolus/PRN doses given</td>
<td>Restart monitoring q30min as above until the target symptom is controlled and then q4hrs thereafter.</td>
<td>Restart monitoring q30min as above until the target symptom is controlled and then q8hrs thereafter.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Restart monitoring q l hr. as above until the target symptom is controlled and then q8hrs thereafter.</td>
</tr>
</tbody>
</table>

* If these medications are used in conjunction with midazolam, then the monitoring suggested by the "midazolam" column applies.

*Nursing support may be through 24/7 telephone access rather than direct monitoring.

**RESOURCES**

- Champlain Regional Palliative Pain and Symptom(s) Management Consultation Service at 1-800- 651-1139 to access palliative care consultants who are available 24/7 for the Champlain Region.
- The Champlain Community Care Access Center at 613-745-5525 for supplies, equipment and assistance in obtaining the medication from your local pharmacies
- eConsult: econsultsupport@lhinworks.on.ca
- Champlain Hospice Palliative Care Program for information about other consultants in the region with palliative care expertise and additional resources: [www.champlainpalliative.ca](http://www.champlainpalliative.ca)
REFERENCES


Canadian Framework for PST use
## Richmond Agitation-Sedation Scale - Palliative version (RASS-PAL)\(^9\)

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Combative</td>
<td>Overtly combative, violent, immediate danger to staff (e.g. throwing items); +/- attempting to get out of bed or chair</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes lines (e.g. IV/SQ/Oxygen tubing) or catheter(s); aggressive, +/- attempting to get out of bed or chair</td>
</tr>
<tr>
<td>+2</td>
<td>Agitated</td>
<td>Frequently non-purposeful movement, +/- attempting to get out of bed or chair</td>
</tr>
<tr>
<td>+1</td>
<td>Restless</td>
<td>Occasionally non-purposeful movement, but movements not aggressive or vigorous</td>
</tr>
<tr>
<td>0</td>
<td>Alert and calm</td>
<td></td>
</tr>
<tr>
<td>-1</td>
<td>Drowsy</td>
<td>Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (10 seconds or longer)</td>
</tr>
<tr>
<td>-2</td>
<td>Light sedation</td>
<td>Briefly awakens with eye contact to voice (less than 10 seconds)</td>
</tr>
<tr>
<td>-3</td>
<td>Moderate sedation</td>
<td>Any movement (eye or body) or eye opening to voice (but no eye contact)</td>
</tr>
<tr>
<td>-4</td>
<td>Deep sedation</td>
<td>No response to voice, but any movement (eye or body) or eye opening to stimulation by light touch</td>
</tr>
<tr>
<td>-5</td>
<td>Not rousable</td>
<td>No response to voice or stimulation by light touch</td>
</tr>
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</table>
Procedure for RASS-PAL Assessment

1. Observe patient for **20 seconds**.
   a. Patient is alert, restless, or agitated **for more than 10 seconds**

   **NOTE:** If patient is alert, restless, or agitated for less than 10 seconds and is otherwise drowsy, then score patient according to your assessment for the majority of the observation period

   Score 0 to +4

2. If not alert, greet patient and call patient by name and say to open eyes and look at speaker.
   b. Patient awakens with sustained eye opening and eye contact (**10 seconds or longer**).

   Score -1

   c. Patient awakens with eye opening and eye contact, but not sustained (**less than 10 seconds**).

   Score -2

   d. Patient has any eye or body movement in response to voice but no eye contact.

   Score -3

3. When no response to verbal stimulation, physically stimulate patient by light touch e.g. gently shake shoulder.
   e. Patient has any eye or body movement to gentle physical stimulation.

   Score -4

   f. Patient has no response to any stimulation.

   Score -5